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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/458,813	12/10/1999	Brian R. Murphy	17634-000330US	9312

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NATIONAL INSTITUTES OF HEALTH
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ROCKVILLE, MD 20852-3804

EXAMINER

CHEN, STACY BROWN

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 11/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/458,813

Applicant(s)

MURPHY ET AL.

Examiner

Stacy B. Chen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 August 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 53-85 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 53-85 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 December 1999 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application. This application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid. Applicant's submission filed on August 26, 2005 has been entered. Claims 53-85 are pending and under examination. The cancellation of claims 1-52 renders all previous rejections of claims 1-52 moot.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 67, 68 and 83-85 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to chimeric viruses, specifically wherein the substitution mutation at position 456 of the L protein is "to another amino acid". The breadth of the claims has not been adequately described such that one of skill in the art would know how to practice the invention.

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The specification describes a mutation wherein the amino acid at position 456 of PIV3 is changed to leucine. However, Applicant's claims encompass a substitution of any of the 20 amino acids. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is one example (456 F) out of 20 possibilities and no particular function. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived.

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3. Claims 62, 77-80 and 84-85 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The subject matter of these claims does not appear to be supported by the specification as filed, in particular the reference to 995 nucleotides. Applicant points to Table 10 at page 108, however, there is no mention of 995 nucleotides. There is an insert of 996 nucleotides. Clarification and correction are required to overcome this rejection.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 53-57, 59-66, 69-73, 75, 81, 82 and 85 are rejected under 35 U.S.C. 102(e) as being anticipated by Belshe *et al.* (US 5,869,036, “Belshe”). These new claims are drawn to subject matter previously claimed. The difference between the previous claim set and the currently claim set is that the L protein is wild type, and the encoded chimeric PIV is attenuated for replication at least 10-fold in the respiratory tract of a primate host infected with said chimeric PIV.

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Belshe teaches hybrid viruses having glycoproteins exchanged between HPIV1, HPIV2 and HPIV3 (as a background genome), see abstract and Example 7, all of record.

Regarding the limitation of 10-fold attenuation of replication, Applicant points to Table 11, page 102, of the specification. Table 11 discloses levels of replication in the upper and lower respiratory tract of hamsters using various constructs of wild type and mutant PIV3 viruses. Applicant's specification teaches that the majority of mutations in the L gene are responsible for the attenuated phenotype of the cp45 virus. Applicant also teaches that other mutations outside of the L gene also contribute to the cp45 attenuated phenotype. While Belshe does not demonstrate levels of attenuated replication, the hybrid viruses that Belshe describes are expected to have the property of attenuated replication of at least 10-fold. One would reasonably expect Belshe's hybrid constructs to have this characteristic because the structural features of the viruses of Belshe and the structural features of Applicant's constructs are the same as claimed. For example, Belshe's cp45 hybrid virus contains the mutation A450T in the F protein. Applicant's construct having the A450T mutation in the F protein had at least a 10-fold attenuation of replication (instant specification, Table 11).

Belshe's construct is a cp45 genome with a wild type L gene introduced. Viruses were recovered and were attenuated, thus demonstrating that the wild type L gene was not entirely responsible for attenuation (Example 5, Belshe). The cp45 genome necessarily contains mutations in genes other than the L gene, thus reading on the instant claims.

Regarding the limitation about the insertion site of the heterologous gene, one would expect that a substitution of HPIV2 HN gene for the background HPIV3 gene would occur

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between the HN and L open reading frames. The claim limitations do not limit the insertion site such that it is distinguished over Belshe.

Given the disclosure of Belshe and the breadth of the instant claims, the claims are anticipated by Belshe.

Claim Rejections - 35 USC § 103

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 58, 68, 74 and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Belshe. The claims encompass gene insertions between a gene start and a gene end sequence of the PIV background genome. This limitation does not lend patentability to the claimed invention because insertion of heterologous gene encoding the antigenic determinant would only be appropriate between a gene start and gene end sequence. One would have been motivated to use the gene start and gene end sequences of Belshe's background PIV in order to retain as much stability as possible when expressing the heterologous genes. One would have had a reasonable expectation of success given the fundamental nature of recombination and the desire to obtain stable expression. Therefore, the claimed subject matter would have been obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

6. Applicant's arguments and observations are primarily directed to the following:

- Applicant discloses that the recovery of Belshe's hybrid *cp45* viruses was performed by a complementation assay wherein a plasmid expressing wild-type HPIV3 L protein provided a very small degree of recovery of virus plaques.
 - In response to this observation, the examiner agrees that the viruses were recovered. Regardless of the amount recovered, Belshe did recover virus (col. 8, lines 21-25). The claims do not require a particular amount of virus be produced.
- Applicant points out that Belshe's disclosure regarding hybrid *cp45* viruses is limited to Example 7, and the mention of exchanging heterologous surface glycoproteins for those on the PIV genome.
 - In response to this observation, the specification describes a method of making the virus using the *cp45* virus genome as a background genome into which other genes may be inserted (co. 9-10).
- Applicant points out that Belshe's explanation for attenuation is mutation of the L protein, not the wild-type. Applicant asserts that Belshe does not contemplate any attenuated virus obtained by mutating other than the L protein. In contrast, Applicant's claims are directed to embodiments wherein the L protein is the wild-type, and the virus remains attenuated due to other temperature-sensitive mutations.
 - In response to this observation, Example 5 of the Belshe patent discloses the introduction of the wild type L gene into the *cp45* genome. Belshe recovered virus that contained a wild type L gene and also contained mutation in gene other than the L gene. Because the *cp45* genome necessarily contains mutations in other genes besides the L gene, the introduction of the wild type L gene resulted

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in a virus that expressed the wild type L protein along with the other mutations that are naturally present in the *cp45* virus (col. 8, lines 21-25).

- Applicant argues that claims 59-74 should not be rejected over Belshe because Belshe does not teach the insertion of genes in the recited positions.
 - In response to this argument, insertion of a heterologous HN protein from HPIV2 into HPIV3, for example, would occur between HN and L open reading frames. The claim limitations do not limit the insertion site such that it is distinguished over Belshe.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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Claims 53-85 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 144-215 of copending Application No. 09/083,793. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is encompasses the embodiments set forth in the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 53-85 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-30 and 46-74 of copending Application No. 09/459,062. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is encompasses the embodiments set forth in the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. Claims 53-85 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 84-163 of copending Application No. 09/586,479. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is encompasses the embodiments set forth in the instant claims.

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This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 53-85 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 180-222 of copending Application No. 09/733,692. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is a species of the instantly claimed genus of PIVs, rendering the genus claims obvious.

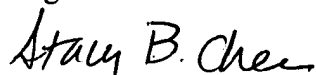
This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

11. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.



Stacy B. Chen
November 10, 2005